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EXAMINER

KOSACK, JOSEPH R

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte NICOLETTA ALMIRANTE, PIERO DEL SOLDATO,
and ENNIO ONGINI

Appeal 2011-003949
Application 10/566,292
Technology Center 1600

Before TONI R. SCHEINER, DONALD E. ADAMS, and
STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a compound, methods of treatment, a pharmaceutical composition, and a pharmaceutical kit. The Patent Examiner rejected the claims on the ground of obviousness. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The invention relates to Angiotensin II Receptor Blocker (ARB) derivatives, said to be useful for the treatment of cardiovascular and other syndromes. (Spec. 1, ll. 4-10.) Claims 1, 2, 5-15, and 18 are on appeal.

The Examiner explains that examination was limited to one species of compound within the claimed genus:

An election of species was made in the application and the Appellant elected without traverse the species 2-butyl-4-chloro-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-imidazole-5-methanol 4-nitroxybutanoic acid ester. As a rejection was made on the elected species, the provisional election was given effect and the search was limited to the elected species. The species is the drug known by the generic name losartan with a 4-nitrooxybutyl ester tail attached to the 5-methanol substitution on the imidazole ring as is represented by the structure

(Ans. 5-6.)

Appellants note that the elected species is “compound (2) . . . a derivative of losartan, whereby an ONO₂ group is attached to the base molecule via a spacer group, which the Examiner refers to as a nitrooxy tether.” (App. Br. 5.)

A copy of the appealed claims may be found in Appendix I of the amended Appeal Brief filed July 9, 2010. (App. Br. 9-17.) The Examiner rejected claims 1, 2, 5-15, and 18 under 35 U.S.C. § 103(a) as unpatentable over McIntyre,¹ Del Soldato I,² and Del Soldato II.³

¹ M. McIntyre et al., *Losartan, an Orally Active Angiotensin (AT₁) Receptor Antagonist: A Review of Its Efficacy and Safety in Essential Hypertension*, 74 PHARMACOL. THER. 181-194 (1997).

² Piero Del Soldato, WO 00/61537 (Oct. 19, 2000).

OBVIOUSNESS

The Issue

The Examiner's position is that losartan was a known drug, and that because Del Soldato I taught that adding a nitrooxy tether to losartan, among others, would reduce side effects for patients affected by oxidative stress or endothelial dysfunctions, or for the elderly in general, it would have been obvious to do so. (Ans. 4-5.)

Appellants "disagree with the Examiner's determination of the scope and content of the prior art." (App. Br. 5.) First, "Del Soldato I discloses losartan amongst several different classes drugs that show lower activity and/or higher toxicity in oxidative stress associated with various pathological conditions (pages 1-7 of Del Soldato I) and does not disclose or teach that losartan can be nitrooxy-modified." (*Id.*) Second, "Del Soldato I discloses losartan along with several hundreds of drugs that may be used as a precursor drug for preparing the compounds of Del Soldato I. In this case, page 41 of Del Soldato I discloses losartan along with a vast number of other drugs listed on page 38 through page 49." (*Id.*) Third, "Del Soldato I discloses that for a drug to be selected as a precursor drug, it must meet at least one of the following 3 tests: NEM test (test 1), CIP test (test 2), and L-NAME test (test 3) (pages 13-16 and pages 27-32)." (*Id.* at 6.) Del Soldato disclosed that some of the drugs it listed did not pass testing, "the skilled artisan would have to test each and every drug listed on pages 38-49 to decide whether it would qualify as a precursor drug." (*Id.*) Accordingly, Appellants contend that "the mere disclosure of losartan as one of several

³ Piero Del Soldato, WO 95/09831 (April 13, 1995).

hundreds of potential precursor drugs does not specifically teach or suggest that losartan can be modified by attaching a nitrooxy tether,” and “the skilled artisan would not have been motivated to select losartan for attaching a nitrooxy tether.” (*Id.*)

The issue with respect to this rejection is whether Del Soldato I suggested modifying losartan with a nitrooxy tether.

Findings of Fact

1. We adopt the Examiner’s findings.

Principles of Law

“The presence or absence of a motivation to combine references . . . is a pure question of fact.” *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). Motivation to apply prior art teachings may be found when “the nature of the problem called for exactly the solutions in the prior art.” *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 411 F.3d 1332, 1338-1339 (Fed. Cir. 2005) (affirming obviousness). *Accord, DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1366 (Fed. Cir. 2006) (“the ‘evidence’ of motive will likely consist of an *explanation* of the well-known principle or problem-solving strategy to be applied”). The prior art’s disclosure of a multitude of combinations does not necessarily render any particular formulation less obvious. *Merck & Co., Inc. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989).

Analysis

Appellants' Specification states that an object of the invention was to reduce side effects of drugs such as losartan. (Spec. 1, ll. 28-30.) There is no dispute that losartan was a known compound. A solution to the side effect problem had been described by Del Soldato I: assess losartan by means of one of three tests, and if it passes one, add a nitrooxy tether and convert the losartan to a derivative having reduced side effects. Del Soldato I taught "the problem-solving strategy to be applied," thus motivating one of skill in the art to use it. *See DyStar*, 464 F.3d at 1366. This is a situation where "the nature of the problem called for exactly the solution[] in the prior art." *Princeton Biochemicals*, 411 F.3d at 1339. Appellants contend that because Del Soldato I said hundreds of known compounds could be modified, none of the modified compounds would have been obvious (save possibly some working examples). Del Soldato I taught screening compounds including losartan, and nitroxyfying those passing the screen, to make a compound having reduced side effects. Del Soldato I suggested hundreds of modified compounds, but that doesn't mean all including losartan were nonobvious. *See Merck & Co.*, 874 F.2d at 807.

Del Soldato I set out specific instructions, and a specific route to the compounds it suggested. In other words, Del Soldato I did more than provide a general approach that might or might not be promising, and Del Soldato I's specific instructions did not involve varying parameters with numerous possible choices. Thus the rejection was not contaminated with the kind of "obvious to try" analysis that results in hindsight. *See In re O' Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988) (obviousness finding appropriate where the prior art "contained detailed enabling methodology for practicing

the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful”).

Claims 2, 5-15, and 18 have not been argued separately and therefore fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

SUMMARY

We affirm the rejection of claims 1, 2, 5-15, and 18 under 35 U.S.C. § 103(a) as unpatentable over McIntyre, Del Soldato I, and Del Soldato II.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

cdc